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EXAMINER	
BERTAGNA, ANGELA MARIE	
ART UNIT	PAPER NUMBER
1637	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/553,376	INOSE ET AL.	
	Examiner	Art Unit	
	Angela M. Bertagna	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 December 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,9 and 10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,9 and 10* is/are rejected.

7)☒ Claim(s) *1* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

1. Applicant's response filed on December 28, 2009 is acknowledged. Claims 1-4, 9, and 10 are currently pending. In the response, claims 1, 2, and 4 were amended, and claim 5 was canceled.

The following include new grounds of rejection necessitated in part by Applicant's amendments to the claims. Any previously made rejections not reiterated below have been withdrawn. Applicant's arguments filed on December 28, 2009 have been fully considered, and they were persuasive in part (see "Response to Arguments" section). Since the new grounds of rejection in section 5 were not necessitated by Applicant's amendment, this Office Action is made **NON-FINAL**.

Claim Objections

2. Claim 1 is objected to because of the following informalities: This claim recites "acid acids" in the last line of the claim.

Appropriate correction is required.

Claim Rejections - 35 USC § 112, 2nd paragraph

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 2 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 contains the trademark/trade name Triton X-100. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe a non-ionic surfactant and, accordingly, the identification/description is indefinite.

It is also noted that the amendment of claim 2 to include the generic name associated with the trademark together with the trademark causes the scope of the claim to be unclear, because the generic name recited in the claims can refer to the surfactant from any source (*i.e.*, other brand names having the generic formula recited in claim 2), whereas the term "Triton X-100" requires a particular source. This causes claim 2 to recite a broad limitation and a narrow limitation within the same claim. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter.

1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 1-4, 9, and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Burdick et al. (EP 0 393 744 A1; cited previously) in view of Akane et al. (Biotechniques (1994)

16(2): 235, 237, 238; cited previously) and further in view of Marguet et al. (Extremophiles (1998) 2: 115-122; newly cited).

These claims are drawn to a method for isolating nucleic acids from a blood sample comprising eukaryotic cells. The method comprises dissolving the blood sample in a buffer comprising a surfactant and a salt of a monovalent cation, heating the resulting solution at 80-100°C, performing gel filtration to obtain a solution containing nucleic acids, and amplifying DNA in the obtained solution.

Burdick teaches methods for isolating nucleic acids from whole blood or peripheral blood mononuclear cells (see abstract and Example 2 at column 14, lines 26-44).

Regarding claims 1, 9, and 10, the method of Burdick comprises:

(a) dissolving a sample in a buffer comprising at least one surfactant and at least one salt of a monovalent cation (column 14, lines 32-39),

(b) heating the obtained solution (column 14, lines 39-41 teaches heating at 118°C; column 6, lines 33-37 teach heating at 80-120°C or 95-120°C; column 6, lines 16-19 teach heating at 100°C),

(c) filtering the heated solution (column 6, lines 52-57 and column 14, lines 41-42),

(d) collecting a solution fraction containing nucleic acids (column 6, lines 52-57 and column 14, lines 41-42), and

(e) amplifying an object DNA from the fraction containing nucleic acids by PCR (column 14, line 40 – column 15, line 3).

Further regarding claim 1 and also regarding claim 4, Burdick teaches that the sample is a blood sample that comprises eukaryotic cells (column 14, lines 25-35). Burdick also teaches that

the salt may be selected from a number of monovalent salts including sodium chloride and potassium chloride (column 7, last paragraph – column 8, first paragraph).

Regarding claim 2, Burdick teaches that the surfactant is Triton X-100 (column 14, lines 37-38).

Regarding claim 3, Burdick teaches that the salt is NaCl (column 14, lines 38-39 and column 7, last paragraph – column 8, first paragraph).

Burdick teaches filtering the heated solution through a membrane filter (column 6, lines 52-57 and column 14, lines 41-42), but does not teach conducting a gel filtration step as required by claim 1. Also, Burdick teaches using NaCl at a concentration of 0.5 to 1.5 weight percent (86 mM – 257 mM), rather than a value within the claimed concentration range of 0.5 - 2 M.

Akane teaches methods of preparing DNA samples for PCR that comprise a gel filtration step (page 235). Akane teaches that degraded DNA and a hemoglobin derivative (hematin) isolated from forensic samples interfere with PCR amplification (page 235, column 2). Akane further teaches that, although contaminating hematin may be removed by treatment with bovine serum albumin, ultrafiltration, chelating resin treatment, gel filtration or anion-exchange chromatography, degraded DNA may only be removed using gel filtration (page 235, column 2).

Marguet teaches that potassium chloride at concentrations within the claimed concentration range, specifically 0.5 M, 1.0 M, and 2.0 M, reduces DNA degradation at temperatures above the boiling point of water by inhibiting depurination (see abstract, pages 116-120, and Figures 1 & 4-6). Marguet concludes by stating, "Our results have implications for the behavior of DNA at high temperature both *in vitro* and *in vivo*. For example, high concentrations of monovalent or divalent salts should reduce template degradation in PCR experiments. This

could be especially important in the case of experiments involving long exposure of DNA at very high temperature and/or using hyperthermophilic archaeal DNA polymerases (page 121)."

It would have been *prima facie* obvious for one of ordinary skill in the art at the time of invention to incorporate a gel filtration step into the method taught by Burdick. Since the method of Burdick comprised a PCR amplification step following nucleic acid isolation (column 14, lines 41-44), an ordinary artisan would have been motivated to incorporate a gel filtration step, as suggested by Akane, in order to remove any contaminating degraded DNA fragments that would interfere with the PCR. An ordinary artisan would have had a reasonable expectation of success in incorporating a gel filtration step into the method of Burdick since both methods were directed to purification of DNA from forensic samples for PCR analysis.

It also would have been *prima facie* obvious for one of ordinary skill in the art at the time of invention to increase the monovalent salt concentration, *e.g.*, to a concentration within the claimed range, when practicing the methods resulting from the combined teachings of Burdick and Akane. Since Marguet expressly suggested including high concentrations of monovalent or divalent salts in PCR amplification reactions to reduce DNA degradation during the reaction (page 121), an ordinary artisan would have been motivated to increase the monovalent and/or divalent salt concentration to a value within the claimed concentration range with a reasonable expectation of success. Attention is also directed to MPEP 2144.05 II, which states, "Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. '[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.' *In re*

Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (MPEP 2144.05)." Thus, the methods of claims 1-4, 9, and 10 are *prima facie* obvious over Burdick in view of Akane and further in view of Marguet.

Response to Arguments

6. Applicant's arguments filed on December 28, 2009 have been fully considered, and they were persuasive in part.

Rejection under 35 U.S.C. 112, second paragraph

Regarding the rejection of claim 2 under 35 U.S.C. 112, second paragraph, Applicant argues that amendment to claim 2 has obviated the rejection (page 3). This argument was not persuasive, because as discussed above, claim 2 still recites a trademark as a claim limitation. Also, as discussed above, the recitation of a generic name together with a trade name in the same claim renders the scope of claim 2 unclear. Since Applicant's arguments were not persuasive, the rejection has been maintained with modifications to address the claim amendments.

Rejections under 35 U.S.C. 103(a) based on Lurquin, Vosbeck, & Werner

Applicant's arguments, see page 3, regarding the rejection of claims 1, 3, 4, 9, and 10 under 35 U.S.C. 103(a) as being unpatentable in view of the combined teachings of Lurquin, Vosbeck, and Werner, have been fully considered and are persuasive. As noted by Applicant at page 3 of the response, the limitations of claim 5, which was not included in the previous rejection, have been incorporated into independent claim 1. Therefore, Applicant argues, the

cited references do not render obvious the methods of the amended claims. This argument was persuasive, and accordingly, the rejection has been withdrawn. The rejection of claim 2 under 35 U.S.C. 103(a) as being unpatentable in view of the combined teachings of Lurquin, Vosbeck, Werner, and Wilson has also been withdrawn in view of Applicant's arguments at page 3.

Rejection under 35 U.S.C. 103(a) based on Burdick and Akane

Applicant's arguments filed on December 28, 2009 have been fully considered to the extent that they apply to the new grounds of rejection above, where claims 1-4, 9, and 10 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Burdick in view of Akane and further in view of Marguet, but they were not persuasive.

(A) Arguments concerning the previously submitted declaration under 37 CFR 1.132

Applicant first argues that the previously submitted declaration under 37 CFR 1.132 demonstrates that the claimed range of salt concentrations is critical and associated with unexpected results (pages 4-5). Applicant argues that the claims have been limited to blood samples, and therefore, the issue raised previously with respect to the breadth of samples encompassed by the claims compared to the experimental data has been addressed (page 5). With respect to the remarks made previously concerning the heating temperature and incubation times, Applicant refers to the specification at page 6, which states, "Heating temperature is not particularly limited so long as it is a temperature at which a protein can be sufficiently denatured....Heating time is not particularly limited so long as it is a time during which proteins can be sufficiently denatured under the heating condition." Applicant argues that these passages in the specification clearly indicate that the temperature and incubation times are not critical (see

pages 5-6). Regarding the identity of the monovalent salt and surfactant, Applicant argues that, although not all of the monovalent salts and surfactants encompassed by the claims were tested, the ordinary artisan would understand that the results presented in the previously submitted declaration would necessarily extend over the full scope of the claim (see page 6). Finally, regarding the issue of statistical significance of the results presented in the declaration, Applicant argues that the results presented in Table 1 of the previously submitted declaration are dramatic and would immediately be recognized as significant by the ordinary artisan (page 6).

Applicant's remarks regarding the amendment of the claims to recite that the sample is a blood sample are noted. With respect to the type of sample, the claims are now commensurate in scope with the evidence presented in the previously submitted declaration. Applicant's arguments regarding the non-criticality of the incubation time and temperature time are also noted, but in the absence of data, it remains unclear whether the beneficial results described in the declaration would necessarily occur over the full range of incubation temperatures encompassed by the claims, particularly since electrostatic interactions between monovalent salts and biological molecules, such as proteins, are known to influence temperature-induced protein denaturation (see, for example, Benjwal et al. (Biochemistry (2005) 44: 10218-10226; newly cited). For instance, it is not clear that the observed beneficial results would be observed when monovalent salt concentrations at the upper end of the claimed range are used with temperatures at the lower end of the claimed range. Applicant's arguments regarding the identity of the salts and surfactants were not persuasive, because the claims broadly encompass any salt of a monovalent cation (*e.g.*, NaCl, KCl, potassium glutamate, guanidinium hydrochloride) and any surfactant (*e.g.*, nonionic, anionic, zwitterionic, cationic). These diverse molecules will

necessarily have very different effects on protein stability and thermal sensitivity, and, in the absence of additional evidence, it is not at all clear that the beneficial results observed for a single combination (NaCl and Triton X-100) will necessarily extend over the full scope of the claimed methods. Finally, Applicant's remarks regarding statistical significance of the results presented previously have been fully considered and are persuasive. It is clear from the data presented on page 3 of the previously submitted declaration that the results are significant.

(B) Arguments with respect to teaching away in the prior art

Applicant also argues that that the prior art teaches away from the use of the claimed salt concentrations and refers to the previously submitted Chien reference to support this argument (see page 6).

Applicant's arguments with respect to teaching away and negative teachings in the art have been fully considered, but they were not persuasive. As discussed previously, Burdick expressly taught diluting the isolated nucleic acids prior to amplification, and since dilution factors, such as 50-fold or 25-fold, were routinely used in PCR amplification, an ordinary artisan would have had a reasonable expectation of success in practicing the method suggested by the combined teachings of Burdick and Akane and determining a suitable dilution factor via routine experimentation. Also, since salt concentrations that may lead to decreased polymerase activity were also known in the art as evidenced, for example, by the Chien reference cited previously by Applicant, an ordinary artisan would have had a reasonable expectation of success in balancing the optimization of the results-effective variables (*i.e.* the dilution factor and salt concentration) when conducting the routine experimentation suggested by the combined teachings of Burdick

and Akane. Furthermore, as discussed above, the newly cited Marguet reference (Extremophiles 1998) expressly suggests conducting PCR amplification in the presence of high monovalent salt concentrations to reduce DNA degradation during the reaction (page 121).

Conclusion

7. No claims are currently allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANGELA BERTAGNA whose telephone number is (571)272-8291. The examiner can normally be reached on M-F, 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Angela M. Bertagna/
Examiner, Art Unit 1637